UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,748	11/30/2004	So H. Lee	5806SNU-1	7184

22442 7590 10/26/2007

SHERIDAN ROSS PC
1560 BROADWAY
SUITE 1200
DENVER, CO 80202

EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
10/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,748	LEE ET AL.	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *1-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application 10/500,748 is a 371 of PCT/KR01/02304, filed on 12/29/2001

Election/Restrictions

1. Applicant's election of Group II, claims 6-13, drawn to a method of producing a cloned pig having an alpha-l, 3-galactosyltransferase gene knocked out, comprising the recited steps (a) to (e); a porcine nuclear transfer embryo "SNU-P2 [Porcine NT Embryo]", which is prepared according to the steps (a) to (d) of claim 6, and deposited KCTC (Korean Collection for Type Cultures) under accession number KCTC 10146BP; and a vector carrying a nucleic acid sequence corresponding to a part of intron 8, exon 9 and a part of intron 9 of a GT gene, wherein an AvaI-DraIII fragment of said exon 9 is substituted with a nucleic acid sequence encoding a puromycin-resistant gene linked to a SV40 poly(A) sequence, in the reply filed on 08/13/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 6-13 are currently under examination.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Indefiniteness

2. Claim 6-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) The term "a wild-type GT gene" in claim 6 and its dependent claims 7-12 is a relative term, which renders the claim indefinite. The term " a wild-type GT gene " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 6 recites," (b) isolating an alpha-1, 3-galactosyltransferase (GT) gene clone from a pig genomic BAC library, and constructing a gene targeting vector using the isolated GT gene, wherein the vector carries a GT gene modified by substituting a portion of *a wild-type GT gene* with a gene encoding a selectable marker by homologous recombination to suppress expression of *a normal GT protein*". Claims 7-12 depend from claim 6.

Relevant to this issue, the specification does not define what an alpha-1, 3-galactosyltransferase (GT) gene is considered as a wild-type GT gene. It is known in the art that polymorphisms (including splicing variants) of a GT gene exist among individual organisms of the same species, including claimed GT gene of pigs. Therefore, in the absence of clear definition, "a wild-type GT gene" recited in claim 6 is a relative term, which renders the claim indefinite. Similarly, it is unclear what the limitation "a normal GT protein" encompasses.

Furthermore, step (b) of claim 6 is also unclear regarding the nexus between the limitation "homologous recombination" occurring at DNA level and the limitation "to suppress

expression of a normal GT protein" at protein level. In other words, it is unclear with respect to whether the GT gene has been knocked out (i.e. removal or disruption of coding sequence at DNA level) or the expression of the GT gene has been knocked down (i.e. by antisence oligonucleotides or RNA interference, both of which involve annealing of homologous sequences, which is broadly encompassed by the limitation "homologous recombination").

(ii) Claim 8 recites, "The method as set forth in claim 6, wherein the gene targeting vector at the step (b) is constructed not to have an exogenous promoter by *a promoter trap method*". It is not clear what *a promoter trap method* is.

Relevant to this issue, the specification discloses, "To effectively select targeted cells, the vector is constructed not to have exogenous promoters by *a promoter trap method*. The vector comprises a nucleic acid sequence corresponding to a part of intron 8, exon 9 and a part of intron 9 of a GT gene, and a nucleic acid sequence encoding a puromycin-resistant gene linked to a SV40 poly (A) sequence, wherein the puromycin-resistant gene substitutes a nucleic acid sequence corresponding to an AvaI-DraIII fragment of the exon 9. The puromycin-resistant gene linked to SV40 poly (A) is inserted to the exon 9 of the GT gene by homologous recombination, thereby disrupting the GT gene (Fig. 9). The gene targeting vector is introduced into nuclear donor cells using FuGENE 6 mentioned in the method of producing a cloned pig expressing GFP". However, the abovementioned disclosure in specification, including Fig. 9, fails to disclose the involvement of a promoter for disruption of a GT gene via homologous recombination. Therefore, in the absence of guidance in the specification, it is unclear what the claimed promoter trap is in the context of disruption of a GT gene via homologous recombination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

3. Claims 6-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The total lack of enablement rejection of claims 6-13 is based on lack of guidance in the specification of instant application, and the following issues at the claimed priority date of instant application, 12/29/2001: **(i)** the rejection of claim 6-13 based on unpredictability in the art for cell type of nuclear donor used for somatic cell nuclear transfer, **(ii)** the rejection of claim 6-13 based on lack of guidance in how to use claimed cloned pigs with heterozygous knockout of α (1,3)-galactosyltransferase (GT) gene, **(iii)** rejection of claims 9 and 13 based on the absence of disclosure of exon 9 sequences to determine the AvaI-Dra III fragment, and **(iv)** the rejection of claims 11 and 12 based on the requirements for deposit of biological materials .

(i) The claims are broadly drawn to use of any cell type as a nuclear donor. The specification teaches knockout of pig α (1,3)-galactosyltransferase (GT) gene in the content of heterozygote. However, the specification fails to teach a homozygous knockout, which is necessary to carry out the intended use of the pig, which is as an organ donor allowing xenotransplantation in human without hyperacute immune rejection. The specification discloses gene targeting by introduction of GFP gene into pig fetal fibroblast (Example 4), the selection, proliferation and preservation of nuclear donor cells transfected with GFP (Example 5), and preparation of recipient oocytes (Example 6). However, the specification discloses GT-knockout in the context of heterozygote (See paragraph [0052], US 2005/0076399), and nowhere in the specification discloses a homozygous knockout of pig α (1,3)-galactosyltransferase (GT) gene in the recited cloned pigs. Thus, the specification provides no guidance for the production of the claimed pigs or method of making a cloned pig to overcome the art recognized unpredictabilities, as more elaboration provided below.

The art of making transgenic animals by somatic cell nuclear transfer was unpredictable at the time of filing. **Clark** et al. teach that only primary somatic cells have been used successfully as a nuclear donor in gene targeting experiments to produce livestock having a disrupted gene of choice (See page 265, col.2, parag. 1, lines 12-15, Clark et al., Gene targeting in livestock: a preview, *Transgenic Research*, 9:263-275, 2000). In addition, Clark et al. teach that about 45-population doubling are required to generate targeted cells (Clark, page 268, col. 2, parag. 1, lines 1-5). **Denning** et al. teach primary cells have limited proliferation capacity and any genetic modifications and nuclear transfer must be accomplished prior to senescence (See page 222, col. 1, lines 5-8, Denning et al., Gene Targeting from *primary fetal fibroblasts* from sheep and pig, *Cloning and Stem Cells*, 3:221-231, 2001). In a study of sheep and goat primary somatic cells, Denning et al. found that of primary somatic cells, fibroblasts were the only cells that either grew at all from the primary cell source or has sufficient population doublings for the selection required in targeted gene transfer. Sheep primary cell cultures primarily were composed of fibroblasts after the third passage or about 12 doublings (Denning et al., page 224, col. 2, lines 11-13). Further, a comparison of separate Black Welsh sheep primary cell fibroblast cultures showed vast differences in the number of doublings prior to senescence; 110 doublings versus 40 doublings (Denning, page 224, col. 2, lines 16-19). In a similar analysis of pig primary cultures, fibroblasts, as in the sheep study, became the predominant cell-type after three passages, but, unlike sheep, pig fibroblasts underwent a crisis after 40 population doublings and had an unstable karyotype (Denning et al., page 224, col. 2, parag. 4 line 4 to page 225, col. 1, line 8). Additional studies of cell cultures prepare from fetal pig organs (gut, kidney, lung and mesonephros showed that these cells senesced or entered crisis after even fewer doublings than

the fibroblast cultures (Denning et al., page 225, col. 1-2, bridging sentence). The art further taught at the time of filing, that the even if sufficient population doublings could be achieved for selection, many of the pure sheep targeted clones senesced before they could be expanded for nuclear transfer, meaning that targeting frequency was lower than expected (Denning et al., page 228, col. 1-2, bridg. sent.). Similar experiments in pigs demonstrated that all the clones senesced, and no targeted cells for nuclear transfer were obtained. In experiments for the production sheep comprising a disruption of the α-1,3-galactosyltransferase gene, related to the present claims, live births were achieved but the animals died within two weeks of birth (Denning et al., page 230, col. 1, parag. 2, lines 1-8). However, Denning et al. reports that McCreath achieved live birth and survival of two gene targeted sheep with disruptions in different genes (Denning et al., page 230, col. 1, parag. 2, lines 9-12). Denning et al. analyzed the results of both sheep experiments and arrives at the conclusion that it is possible that for gene targeted sheep, the success depends on unknown factors, whereas in pigs, the use of fibroblasts to produce gene-targeted pigs is not possible (Denning et al., page 230, col.1, parag. 1, lines 7-13). Denning continues to state that for sheep the parameters of cell growth and targeting efficiency reported therein just about make feasible the production of gene targeted sheep. For pigs, Denning et al. continues to state that the lower proliferative capacity indicates that gene targeted pigs are only marginally likely. In other words, at the time of filing, the skilled artisan would have regarded the production of gene targeted pigs (and sheep) as being unpredictable requiring an undue amount of experimentation without a predictable degree of success. Further, given that fibroblasts were the only cells shown to divide a sufficient number of times in sheep to provide cells for nuclear transfer, fibroblasts, derived from the mesoderm, would be the only cell useful

for the presently claimed invention (claims 6-13). This is consistent with Applicant's own post-filing publications by **Hyun et al., 2003** (Hyun et al., Production of nuclear transfer-derived piglets using porcine fetal fibroblasts transfected with the enhanced green fluorescent protein. *Biol Reprod.* 69(3): 1060-8, 2003), and **Lee et al., 2005** (Lee et el., Production of transgenic cloned piglets from genetically transformed fetal fibroblasts selected by green fluorescent protein, *Theriogenology,* 63(4): 973-91, 2005)

(ii). As discussed in the above section, the specification fails to support the claimed method of making the cloned pigs with homozygous knockout of α (1,3)-galactosyltransferase (GT) gene, as a relevant issue, the specification also fails to support the use of cloned pigs with heterozygous knockout of α (1,3)-galactosyltransferase (GT) gene. This is because in the heterozygous cloned pigs, the presence of remaining copy of α (1,3)-galactosyltransferase (GT) gene in heterozygous cloned pigs would cause hyperacute immune rejection as an organ donor for the intended use in xenotransplantation to a human. One of skill in the art would not know how to use the claimed heterozygous knockout pig.

(iii). It is noted that the rejection of claims 9 and 13 is based on the absence of disclosure of exon 9 sequences to determine the AvaI-Dra III fragment.

Claims 9 and 13 recite, "wherein an AvaI-DraIII fragment of said exon 9 is substituted with a nucleic acid sequence encoding a puromycin-resistant gene linked to a SV 40 poly (A) sequence". The Examiner notes that the restriction enzyme site of AvaI is C/YCGRG (R: A or G; Y C or T), whereas the restriction enzyme site of DraIII is CACNNN/GTG (N: A or T or G or C). It is noted that the specification discloses neither the size of the claimed AvaI-DraIII fragment of said exon 9 nor the nucleotide sequences of exon 9. In fact, the specification does

not disclose any sequence information of the asserted isolated pig α-l, 3-galactosyltransferase (GT) gene. There is no guidance and/or working example regarding the frequency and locations of AvaI and DraIII restriction enzyme sites within a given pig α-l, 3-galactosyltransferase (GT) gene. As discussed before of the rejection of claims 6-12 under the second paragraph of 35 U.S.C. 112, it is known in the art that polymorphisms (including splicing variants) of a GT gene exist among individual organisms of the same species, including claimed GT gene of pigs. Therefore, in the absence of disclosure of critical information of the asserted isolated pig α-l, 3-galactosyltransferase (GT) gene in the specification, a skilled person in the art cannot determine which fragment is the recited "AvaI-DraIII fragment of said exon 9" to make and use of the claims 9 and 13 of instant application.

(iv). It is noted that the rejection of claims 11 and 12 is based on the rejection of claim 11 and 12 is based on the requirements for deposit of biological materials.

The application contains a porcine nuclear transfer embryo "SUN-P2 [porcine NT embryo]" (claims 11 and 12 of instant application), that is encompassed by the definitions for biological material set forth in 37 C.F.R. § 1.801. Because it is apparent that this porcine nuclear transfer embryo is essential for practicing the claimed invention, they must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809. The applicants' assertion that the embryo is deposited is noted. However, all of the requirements of C.F.R. §§ 1.801 through 1.809 have not been met. In particular, applicants failed to comply with 37 C.F.R. § 1.809(d).

The following is a quotation of 37 C.F.R. § 1.809(d):

" For each deposit made pursuant to these regulations, the specification shall contain: (1) The accession number for the deposit; (2) The date of the deposit; (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and (4) The name and address of the depository."

The specification discloses that the reconstructed embryo is designated "SNU-P2 [Porcine NT Embryo]", and deposited at an international depositary authority, KCTC (Korean Collection for Type Cultures; KRIBB, 52, Oun-dong, Yusong-ku, Taejon, Korea) on Dec. 27, 2001, under accession number KCTC 10146BP (See paragraph [0066], US 2005/0076399).

As a required element, the deposited biological material must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. It is not clear under what conditions the deposit was made; there is no indication that the deposit was made under the Budapest Treaty. If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific embryos have been deposited under the Budapest Treaty and that the deposited material will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

Applicants should also provide statement corroborating that the biological material deposited is a biological material specifically identified in the specification and a statement of viability from the depository.

Thereby, claim 11 and its dependent claim 12 fail to comply with the enablement requirement because the claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Written description

4. Claims 6-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 6 recites," (b) isolating an alpha-1, 3-galactosyltransferase (GT) gene clone from a pig genomic BAC library, and constructing a gene targeting vector using the isolated GT gene, wherein the vector carries *a GT gene* modified by substituting a portion of a wild-type GT gene with a gene encoding a selectable marker by homologous recombination to suppress expression of a normal GT protein". Claims 7-12 depend from claim 6.

Claim 13, an independent claim, recites, "A vector carrying a nucleic acid sequence corresponding to a part of intron 8, exon 9 and a part of intron 9 of *a GT gene*, wherein an AvaI-DraIII fragment of said exon 9 is substituted with a nucleic acid sequence encoding a puromycin-resistant gene linked to a SV 40 poly(A) sequence".

The claims are directed a method of producing a cloned pig having an alpha-1,3-galactosyltransferase (GT) gene knockout; a vector comprising a GT gene wherein part of the

GT gene being replaced with puromycin-resistant gene. The specification discloses a GT gene being a pig alpha-1, 3-galactosyltransferase (GT) gene.

The nucleotide sequences that encode "a GT gene", variants, and fragments thereof encompassed within the genus of a vector comprising "a GT gene" have not been disclosed. Based upon the prior art there is expected to be variation among the species of cDNA, which encode an alpha-1,3-galactosyltransferase, because the sequence of alpha-1,3-galactosyltransferase cDNAs would be expected to vary among individuals. The specification discloses isolation of a pig GT gene by screening a pig genomic BAC library, but does not disclose other mammalian GT gene cDNAs or GT gene cDNAs from other cell types. There is no evidence on the record of a relationship between the structure of any GT gene cDNA and the claimed pig GT gene cDNA that would provide any reliable information about the structure of other GT gene cDNAs within the genus. There is no evidence on the record that the asserted pig GT cDNA had a known structural relationship to any other GT gene cDNAs sequences from other species; the specification only asserted the isolation of a single pig GT gene cDNA obtained from an undisclosed origin, but no corresponding cDNA sequences have been disclosed in the specification; the art indicated that there is variation between GT gene cDNA sequences and their functions. The specification has not even disclosed the type of GT genes (which includes splicing variants) that the claimed cDNA encodes. There is no evidence of record that would indicate that any of the claimed variants and fragments of the isolated pig GT gene, encompassed by claim 13 of instant application, have the biological activity of a GT gene. In the absence of a functional assay it would not be possible to test variants of the claimed sequences for biological activity. Also with regard to the claimed allelic variants, encompassed by claim 13

of instant application, the skilled artisan cannot envision the structure of such a variant because such variants are randomly produced in nature, and cannot be predicted from a known sequence. The specification does not teach any characteristics of an "allelic" variant that would distinguish it from a non-natural variant constructed by the hand of man. In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus, because a pig GT gene cDNA clone not representative of the claimed genus. Consequently, since Applicant was in possession of only an unspecified pig GT gene cDNA clone and since the art recognized variation among the species of the genus of cDNAs that encode GT genes, the pig GT gene cDNA was not representative of the claimed genus. Therefore, Applicant was not in possession of the genus of lipase cDNAs as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

5. **(a).** Prior arts relevant to the claimed invention are listed below.

(1). Damiani et al. (US patent No. 6,700,037, issued 2004, filed 12/28/2000)

(2). D'Apice et al. (US patent No. 6,849,448, issued Feb. 1, 2005, filed 12/4/1997)

(3). Suzuki et al., Construction and evaluation of a porcine bacterial artificial chromosome library. *Anim Genet.* 31(1): 8-12, 2000

(b). Posting filing arts relevant to the claimed invention are listed below.

(1). Dai et al. Targeted disruption of the alpha1, 3-galactosyltransferase gene in cloned pigs. *Nat Biotechnol.* 20(3): 251-5, 2002.

(2). Kolber-Simonds et al., Production of alpha-1,3-galactosyltransferase null pigs by means of nuclear transfer with fibroblasts bearing loss of heterozygosity mutations. *Proc Natl Acad Sci U S A.* 2004 May 11;101(19):7335-40, 2004.

(3). Ramsoondar et al., Production of alpha 1,3-galactosyltransferase-knockout cloned pigs expressing human alpha 1,2-fucosylosyltransferase. *Biol Reprod.* 69(2): 437-45, 2003.

(4). Hawley, US publication number 2006/0242722 (US application number 10/524,381)

Conclusion

6. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent

Examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Wu-Cheng Winston Shen, Ph. D.
Patent Examiner
Art Unit 1632

/Valarie Bertoglio, Ph.D./
Primary Examiner
AU 1632